UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/602,778	06/23/2000	Cynthia C. Bamdad	M1015/7002 TJO	9746

7590 09/25/2003

Timothy J. Oyer
c/o Wolf, Greenfield & Sacks, P.C.
Federal Reserve Plaza
600 Atlantic Avenue
Boston, MA 02210-2211

EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/25/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/602,778	BAMDAD ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- Th MAILING DATE of this communication app ars on the cov r sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-8,13-15,18-38,60-70,185-190,192,206 and 213-226* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-8,13-15,18-38,60-70,185-190,192,206 and 213-226* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

The amendment filed July 9, 2003 is acknowledged and has been entered.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 3-8, 13-15, 18-38, 60-70, 185-190, 192, 206 and 213-226 in Paper No. 17 is acknowledged.

Note: Applicant's assessment of claims 60, 185-190 and 192 is corrected. Examiner, inadvertently excluded these claims from Group I. Therefore, Group I includes claims 60, 185-190 and 192.

Priority

2. If applicant desires priority under 35 U.S.C. 119 (e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3-8, 13-15, 18-38, 60-70, 185-190, 192, 206, and 213-226 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 35 is vague and indefinite because it is unclear if the first and second magnetic beads have the same type of agent linked to them of different types of agents linked to them. Furthermore, it is unclear how to differentiate the linkage of the particle to the first bead versus the second bead. Do the beads posses some physical difference that allows for the differentiation.

Claim 37 is vague and indefinite because it is unclear if the first suspected binding partner is the same as the second suspected binding partner. Furthermore, do the colloidal particle posses different types of signal entities which allow for the differentiation?

Claim 60, lines 1 and 11 the recitation "relative to" is vague and indefinite.

The term "relative to" in claim 60, lines 1 and 11 is a relative term which renders the claim indefinite. The term "relative to" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary

skill in the art would not be reasonably apprised of the scope of the invention. Does the colloid particle bind to the non-colloidal structure or are the colloid particle and the non-colloidal structure in close proximity to each other?

Claim 60 is vague and indefinite because it is unclear if there is a sample of analyte used in the method. It appears applicant is using known reagents for specific binding events however, there are no steps involving the addition of an unknown sample. Further, it is unclear what happens to the unbound reagents are they removed by a separation step or do the unbound reagents remain there? See also deficiency found in claim 206.

Claim 60 is vague and indefinite because it is unclear how the non-colloidal structure and the colloidal particle become immobilized with respect to each other (i.e. does the agent specifically bind to the binding partner of the colloidal particle or does the agent bind an analyte and the binding partner bind to the same analyte to form a complex, because as recited the claims not only read on a biological or chemical agent linked to a colloidal particle but also appears to read on a binding partner adapted to bind to the particle. See also deficiency found in claim 206.

Claim 60 is vague and indefinite because of the recitation "self assembled monolayer of a plurality of molecules thereon". It is unclear what role the plurality of molecules play. Also it is unclear what relationship exits between the plurality of molecules and the binding partner. Furthermore, does the addition of the self-assembled monolayer expose the binding partner or does it block the binding partner? See also deficiency found in claim 206.

Claim 60 line 14 the recitation "auxiliary" is vague and indefinite. It is unclear if this is the only signal generated or is there another signal. Furthermore, it is unclear if this signal entity is detected or not? Does the detection of the signal entity determine the binding of the bead and particle to determine immobilization of the colloid particle relative to the non-colloidal structure? See also deficiency found in claim 206.

Claim 66 the recitation "can be" is vague and indefinite. The phrase "can be" is a conditional phrase and is not a positive recitation.

Claim 206, line 6 the recitation "non-colloidal structure" there is insufficient antecedent basis for this limitation.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claim 206, 213 are rejected under 35 U.S.C. 102(e) as being anticipated by Bamdad et al (US 6,541,167).

Bamdad et al disclose a method for detecting a complex in which a transfer particle (non-colloidal structure) with a binding ligand which binds to a target analyte. Bamdad et al disclose that this transfer particle can be a magnetic particle (col 4, lines 34-35). Bamdad et al disclose that a reporter particle (colloidal particle) with a binding ligand. Bamdad et al disclose that the reporter particle also binds to the analyte to form a complex of transfer particle, analyte and reporter particle (col 2, lines 39-67 and Figure 1A). Bamdad et al disclose that the reporter particle can comprise a self-assembled monolayer and electron transfer moieties (signal entities). Bamdad et al disclose that the monolayer can be mixed (col 12).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 3-8, 13, 14, 18-20, 22, 26-28, 61, 62, 192, 206, 213, 215,218 and 219 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,617) in view of Dremel (WO 98/34114).

Bamdad et al disclose a method for detecting a complex in which a transfer particle (non-colloidal structure) comprises a binding ligand (agent) which binds to a target analyte. Bamdad et al disclose that this transfer particle can be a magnetic particle (col 4, lines 34-35). Bamdad et al disclose that a reporter particle (colloidal particle) comprises a binding ligand. Bamdad et al disclose that the reporter particle also binds to the analyte to form a complex of transfer particle, analyte and reporter particle (col 2, lines 39-67 and Figure 1A). Bamdad et al disclose that the reporter particle can comprise a self-assembled monolayer and electron transfer moieties (signal entities). Bamdad et al disclose that the monolayer can be mixed (col 12). Bamdad et al disclose that the signal entity can comprise ferrocene. Bamdad et al discloses the anlayte can be a drug.

Bamdad et al differ from the instant invention in failing to teach the direct application of the analyte (binding partner) to the particle.

Dremel et al disclose non-magnetic particles coated with the analyte to be determined. Dremel et al disclose that this application provides for direct determination of the analyte.

It would have been obvious to one of ordinary skill in the art to incorporate analyte coated non-magnetic particles as taught by Dremel et al into the method of Bamdad et al because Dremel et al shows that this application provides for direct determination of the analyte and thus would allow for a more precise and sensitive assay.

11. Claim 15 and 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al and Dremel in view of Charych et al (US 6,001,556).

See above for teachings of Bamdad et al and Dremel.

Bamdad et al and Dremel differ from the instant invention in failing to teach allowing the colloidal particle the ability to fasten to the non-colloidal structure in the presence of a candidate drug for interruption of binding of the ligand.

Charych et al disclose a competitive assay in which a drug candidate is introduced into a system containing a receptor and its reciprocal binding partner. Charych et al disclose that if the drug binds to the receptor or modifies the binding partner's binding capacity, there is a decrease in the signal (col 20, lines 1-40). Charych et al disclose that this provides for the development and improvement of drugs

by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand.

It would have been obvious to one of ordinary skill in the art to incorporate candidate drugs and their reagents as taught by Charych et al into the modified method of Bamdad et al because Charych et al shows that that this provides for the development and improvement of drugs by observing competitive inhibition of natural binding events between all surfaces or binding sites and their natural bioactive ligand.

12. Claims 23-25 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,167) and Dremel in view of Charchych and further in view of Hansen et al (US 5,589,401).

See above for teachings of Bamdad et al (US 6,541,617), Dremel and Charchych.

Bamdad et al and Dremel et al differ from the instant invention in failing to teach the use of multiple reagents on multiple different particles.

Hansen et al disclose a method for the simultaneous determination of one or more analytes in a fluid. Hansen et al disclose the use of a plurality of microspheres and reagents which allow for the determination of a plurality of analytes (col 9, line 64 – col 10, line 22). Hansen et al disclose that one can analyze concurrently multiple analytes by using the appropriate reagents (col 9, line 64 – col 10, line 22).

It would have been obvious to one of ordinary skill in the art to incorporate the use of different types of particles and reagents as taught by Hansen et al into the modified method of Bamdad et al because Hansen et al shows that one can analyze concurrently multiple analytes by using the appropriate reagents.

13. Claims 29-33, 185-190 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,167) and Dremel (WO/98/34114) in view of Bamdad et al (US 5,620,850).

See above for teachings of Bamdad (6,541,167) and Dremel.

Bamdad (6,541,167) and Dremel differ from the instant invention failing to teach that the agent or binding partner is adapted for linkage to the non-colloidal structure or particle by a metal binding tag/metal/chelate linkage. Bamdad et a (6,541,167) and Dremel also fail to teach the agent or binding partner carries immobilized thereto a chelate coordinating metal, and at least one of the agent or binding partner is derivatized with a polyamino acid tag.

Bamdad et al (US 5,620,850) disclose metal binding tag/metal/chelate linkers and biomolecules derivatized with a polyamino acid tag, which coordinate the metal ion (see columns 5-8). Bamdad et al (5,620,850) disclose that the use of such tags provide an easily synthesized chemical species that readily adheres to a surface and that facilitates surface immobilization of a binding partner of a molecule desirably captured at the surface with a high degree of sensitivity and minimal to zero non-specific binding. Bamdad et al also disclose that biotin can be combined with protein reagents.

It would have been obvious to one of ordinary skill in the art to incorporate tags as taught by Bamdad et al (5,620,850) into the modified method of Bamdad et al (US 6,541,167) because Bamdad et al (5,620,850) shows that the use of such tags provide an easily synthesized chemical species that readily adheres to a surface and that

facilitates surface immobilization of a binding partner of a molecule desirably captured at the surface with a high degree of sensitivity and minimal to zero non-specific binding.

14. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (6,541,617) and Dremel in view of Altieri (US 6,346,389).

See above for teachings of Bamdad (6,541,617) and Dremel.

Bamdad et al (US 6,541,617) and Dremel differ from the instant invention in failing to teach the binding partner is adapted for linkage to the particle by glutathione/glutathione-s-transferase ligand interaction.

Altieri et al disclose glutathione-s-transferase fusion proteins, which are immobilized onto a glutathione substrate. Altieri et al disclose that this immobilization allows for the separation of protein-protein complexes from uncomplexed forms, as well as to accommodate automation of an assay (col 10, lines 9-36).

It would have been obvious to one of ordinary skill in the art to incorporate glutathione-s-transferase fusion proteins and glutathione substrates as taught by Altieri et al into the modified method of Bamdad et al because Altieri et al disclose that this immobilization allows for the separation of protein-protein complexes from uncomplexed forms, as well as to accommodate automation of an assay.

15. Claims 63-67 rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,617) and Dremel in view of Virtanen (US 6,342,349).

See above for teachings of Bamdad et al and Dremel.

Bamdad et al and Dremel differ from the instant invention in failing to teach the presence of an enzyme having the ability to cleave the agent or binding partner.

Virtanen discloses an immunoassay method comprising the immobilization of solid phases. Virtanen discloses that the solid phases comprise binding partner and are exposed to cleavable spacer molecules, which comprise cleavage sites. (see figures 1 and 3). Virtanen also discloses that the cleavable spacer molecules bind to both the solid phases. Virtanen discloses that enzymes can be used as cleavage reagents by incorporating into the spacer a moiety that serves as the substrate (enzyme substrate) for the given enzyme (col 34, lines 15-17). Virtanen discloses that the analyte can be a drug candidate (col 55, line 53 – col 56, line 67). Virtanen discloses that the cleavable spacer molecules also comprise antibodies specific for the analyte of interest. Virtanen discloses that when the analyte (drug candidate) is present it binds to the antibody and prevents the chemical cleaving agent (enzyme) from cleaving the solid phases. Virtanen discloses that the use of cleavable spacers and enzymes provide the advantages. First, all components are immobilized onto the assay site during manufacturing. Second, as a consequence of immobilization, less reagents are needed. Third, the kinetics are improved, because all components are maintained in close proximity to one another.

It would have been obvious to one of ordinary skill in the art to incorporate cleavage spacers and enzymes as taught by Virtanen into the modified method of Bamdad et al (6,541,617) because Virtanen shows that the use of cleavable spacers and enzymes provide the advantages. First, all components are immobilized onto the assay site during manufacturing. Second, as a consequence of immobilization, less

reagents are needed. Third, the kinetics are improved, because all components are maintained in close proximity to one another.

16. Claims 68-70, 214, 216, 217, 220-226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bamdad et al (US 6,541,617) and Dremel in view of Virtanen as applied to claims 3-8, 13, 14, 18-20, 22, 26-28, 61-67, 192, 206, 213, 215,218 and 219 above, and further in view of Bamdad et al et al (US 5,620,850).

See above for teachings of Bamdad (6,541,167), Dremel and Virtanen.

Bamdad (6,541,167) and Dremel differ from the instant invention failing to teach that the agent or binding partner is adapted for linkage to the non-colloidal structure or particle by a metal binding tag/metal/chelate linkage.

Bamdad et al (US 5,620,850) disclose metal binding tag/metal/chelate linkers and biomolecules derivatized with a polyamino acid tag, which coordinate the metal ion (see columns 5-8). Bamdad et al (5,620,850) disclose that the use of such tags provide an easily synthesized chemical species that readily adheres to a surface and that facilitates surface immobilization of a binding partner of a molecule desirably captured at the surface with a high degree of sensitivity and minimal to zero non-specific binding. Bamdad et al also disclose that biotin can be combined with protein reagents.

It would have been obvious to one of ordinary skill in the art to incorporate tags as taught by Bamdad et al (5,620,850) into the modified method of Bamdad et al (US 6,541,167) because Bamdad et al (5,620,850) shows that the use of such tags provide an easily synthesized chemical species that readily adheres to a surface and that

facilitates surface immobilization of a binding partner of a molecule desirably captured at the surface with a high degree of sensitivity and minimal to zero non-specific binding.

Conclusion

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Giaever (US 4,115,535) discloses magnetic beads comprising a binding partner and non-magnetic beads comprising a binding partner. The binding partners of the beads bind to an analyte of interest to form a complex.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
September 11, 2003

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

09/19/03